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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	**PAPER NUMBER**
1642	
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11/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,408	SUTHANTHIRAN ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-13 and 15-20* is/are pending in the application.

4a) Of the above claim(s) *3-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 13 and 15-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/07/2007 has been entered.

Claims 1, 3-13 and 15-20 are pending.

Claims 3-12 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 1, 13 and 15-20 are currently under consideration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Griswold et al. (US 5,824,696, 1998).

Griswold et al. teach a method of treating chronic inflammatory disease states in a mammal, especially a human, comprising administering an effective amount of an angiotensin II receptor antagonist (column 1, lines 66 to column 2, line 1). Specifically, the patent teaches a method of treating disorders such as tumor growth, i.e., neoplastic transformation and growth/metastasis (column 2, lines 6-12). With regards to the angiotensin II receptor antagonist, the patent teaches that angiotensin antagonists include, but are not limited to, the AT1 antagonist losartan (column 3, lines 14-17).

In response to this rejection, Applicants assert that Griswold et al. doe not teach the claimed method for reducing formation, progression or metastasis of a neoplasm, but instead, speculates "... that this tissue (synovial cells) is reactive and proliferates in response to injury may reflect a broader role for angiotensin in the regulation of tissue injury, proliferation and differentiation." Thus, Applicants assert that the mere speculation in Griswold et al. does not properly substitute for the teaching that is required in MPEP 2131 for an anticipation rejection. Secondly, Applicants assert that what ever it is that Griswold et al. speculates about in column 2, lines 10-12, e.g., "As such this would include the treatment of disorders such as tumor growth...", is not understandable to one of skill in the art. For example, Applicants assert that Griswold appears to suggest that something "includes treatment of disorders such as tumor growth". However, Applicants contend that what that something is, however is a mystery. More importantly, what the treatment would be is also a mystery; and therefore, a person having ordinary skill does not learn from Griswold et al. what "... would include treatment of disorders such as tumor growth...".

These arguments have been carefully considered, but are not found persuasive.

First, the Examiner acknowledges and does not dispute the requirements set forth in MPEP 2131 for an anticipation rejection. However, the Examiner recognizes that while "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir.1987), a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989), see MPEP 2123. Thus, while Applicants focus the majority of their arguments on Griswold et al.'s use of the term "speculates", the Examiner recognizes that these teachings would have reasonably suggested to one having ordinary skill in the art a method of treating a chronic inflammatory condition such as tumor growth, i.e., neoplastic transformation and growth/metastasis. Similarly, regarding Applicants contention that it is not understandable to one of skill in the art what that something includes, the Examiner acknowledges that upon reading this particular section one of skill in the art would be unclear what the something is. However, the Examiner recognizes that when the Griswold patent is viewed a whole one of skill in the art would clearly recognizes the something is the method taught by Griswold, e.g., a method of treating a

chronic inflammatory syndrome such as cancer. For example, the Griswold reference, as a whole, is drawn to a method of treating chronic inflammatory disease states in a mammal, especially a human, comprising administering an effective amount of an angiotensin II receptor antagonist (column 1, lines 66 to column 2, line 1), which is not disputed by Applicants (see remarks 11/06/2006, page 8). Moreover, as stated by Applicants, Griswold teaches the following:

> "The observation of the presence of Angiotensin II receptors on synovial cells gives rise to the speculation that this tissue which is reactive and proliferates in response to injury may reflect a broader role for angiotensin in the regulation of tissue injury, proliferation and differentiation. As such this would include treatment of disorders such as tumor growth, i.e. neoplastic transformation and growth/metasis, bone marrow maturation and differentiation, skin maturation and differentiation, and hepatocyte maturation and differentiation. Chronic inflammatory diseases would also include the proliferative lymphocyte responses, such as inflammatory auto immune diseases (preferably other than psoriasis and other topical skin disorders), systemic lupus erythrematous, rheumatoid arthritis and diabetes. Chronic inflammatory diseases also include the connective tissue disorders such as Sjogrens disease, multiple sclerosis, scloderma, and the mixed connective tissue disorders which include multiple organs, such as the kidney, thyroid and salivary glands. Chronic inflammatory diseases also include disorders such as inflamed joints, rheumatoid arthritis, rheumatoid spondylitis, and gouty arthritis and the various other arthritic conditions such as osteoarthritis and chondromalacia patellae. Chondromalacia, or destruction of cartilage is a characteristic present in inflammatory conditions of the joint. It is also recognized that while osteoarthritis is not considered an inflammatory condition, per se, it is included as an arthritic condition for the purposes herein." (column 2, lines 6-32)

Thus, one of skill in the art would reasonably conclude that "this" (underlined above for emphasis) includes embodiments encompassed by the Griswold's invention, since in the third line, fourth line and fifth line of this section Griswold teaches that "Chronic inflammatory diseases would also include...." In other words, while not explicitly stating that disorders such as tumor growth is a chronic inflammatory condition, it would be clear to one of ordinary skill in the art upon reading the reference as a whole that treating chronic inflammatory conditions would encompass treatment of tumor growth.

Claims 1 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by De Gasparo et al. (WO 97/31634 A1, 1997).

De Gasparo et al. teach a method of treating pathogical symptoms which are substantially reduced, halted or prevented by apoptosis, which comprises administering a therapeutically effective quantity of an AT1 receptor antagonist (page 13, 3rd full paragraph). With regards to pathological

symptoms which are substantially reduced, halted or prevented by apoptosis, the WO document teaches that apoptosis occurs, for example, in malignant tumors, with the growth of these tumor frequently being retarded (page 12, 4th full paragraph). With regards to the AT1 receptor antagonist, the WO document teaches that the AT1 receptor antagonist include, but are not limited to, small molecules such as Valsartan and/or Losartan (page 2).

Claims 1, 13, 17 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Bullock et al. (US 6,465,502, filed 12/21/1999) as evidenced by De Gasparo et al. (WO 9731634 A1, 1997) and Kassiotis et al. (J. Exp. Med. 2001; 193: 427-434).

Bullock et a. teach a method of treating lung cancer comprising administering a therapeutically effective amount of valsartan to a patient in need thereof (Column 23-24, claim 1 of US patent). The patent further teaches that the treatment should be considered as a palliative therapy with other biological response modifies such as tumor necrosis factors (column 9, lines 44-50). Thus, while Bullock et al. does not explicitly teach that valsartan is a AT1 receptor antagonist, the claimed limitation does not appear to result in a manipulative difference because as evidenced by De Gasparo et al. Valsartan is an angiotensin II antagonist which binds to the AT1 receptor subtype (1st page, last paragraph to page 2). Moreover, although Bullock et al. does not explicitly teach that the tumor is associated with immunosuppressive therapy, the claimed limitation does not appear to result in a manipulative difference between the prior art because as evidenced by Kassiotis et al tumor necrosis factor exhibits potent immunosuppressive properties (abstract). As such, Bullocks method which encompasses an AT1 receptor subtype antagonist as a palliative therapy with tumor necrosis factors meets the claimed limitation

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bullock et al. (US 6,465,502, filed 12/21/1999) as evidenced by De Gasparo et al. (WO 9731634 A1, 1997) and Kassiotis et al. (J. Exp. Med. 2001; 193: 427-434), as applied to claims 1, 13, 17 and 20 above, in view of Pham et al. (Ann. Thoradic Surgery 1995; 60: 1623-1626).

Bullock et a. teach a method of treating lung cancer comprising administering a therapeutically effective amount of valsartan to a patient in need thereof (Column 23-24, claim 1 of US patent). The patent further teaches that the treatment should be considered as a palliative therapy with other biological response modifies such as tumor necrosis factors (column 9, lines 44-50). In addition to being useful as a palliative therapy, Bullock et al. teach that valsartan is useful as an adjuvant therapy in combination with surgery (column 9, lines 44-46)

Bullock et al. does not explicitly teach that the patient is a transplant recipient.

Pham et al. teaches that prolonged nonspecific immunosuppressive therapy after solid-organ transplantation is associated with an increased risk of certain cancers (page 1623, 1st column, 1st full paragraph). In particular, the reference teaches that skin and lung tumors are the most frequent solid tumors in heart transplant recipients, wherein skin tumors usually have a benign course, whereas lung and other solid tumors developing in cardiac transplant recipients carry a poor prognosis (page 1623, Conclusion).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to administer valsartan as taught by Bullock et al. to a heart transplant recipient in view of the teachings of Pham et al.. One would have been motivated to do so because Pham et al. teach that skin and lung tumors are the most frequent solid tumors in heart transplant recipients, wherein skin tumors usually have a benign course, whereas lung and other solid tumors developing in cardiac transplant recipients carry a poor prognosis. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by administering valsartan as taught by Bullock et al. to a heart transplant recipient in view of the teachings of Pham et al., one would achieve a method of treating lung cancer in a heart transplant recipient.

Claims 16 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bullock et al. (US 6,465,502, filed 12/21/1999) as evidenced by De Gasparo et al. (WO 9731634 A1, 1997) and

Kassiotis et al. (J. Exp. Med. 2001; 193: 427-434), as applied to claims 1, 13, 17 and 20 above, in view of Penn (Ann. Rev. Med. 1988; 39: 63-73).

Bullock et a. teach a method of treating lung cancer comprising administering a therapeutically effective amount of valsartan to a patient in need thereof (Column 23-24, claim 1 of US patent). The patent further teaches that the treatment should be considered as a palliative therapy with other biological response modifies such as tumor necrosis factors (column 9, lines 44-50).

Bullock et al. does not explicitly teach that the patient has an autoimmune disorder.

Penn teaches that immunosuppressive agents used to suppress immunity and inflammatory responses in a large number of autoimmune disorders increase the incidence of cancer (page 66, last paragraph bridging page 67).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to administer valsartan as taught by Bullock et al. to a patient with a autoimmune disease in view of the teachings of Penn. One would have been motivated to do so because Penn teaches that immunosuppressive agents used to suppress immunity and inflammatory responses in a large number of autoimmune disorders increase the incidence of cancer. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by administering valsartan as taught by Bullock et al. to a heart transplant recipient in view of the teachings of Penn, one would achieve a method of treating cancer in a patient suffering from an autoimmune disorder.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 13 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-8 and 10 of U.S. Patent No. 6,641,811.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the method for reducing formation, progression or metastasis of a neoplasm in conjunction with immnosuppressive therapy in a mammal in need thereof, comprising treating the mammal with an effective amount of an angiotensin II receptor blocker claimed in the conflicting patent appears to fall with in the same scope of a method for reducing formation, progression or metastasis of a neoplasm, comprising administering an effective amount of an angiotensin II receptor type II AT1 antagonist, claimed in the instant application.

Note: The transitional term "comprising" recited in the currently pending claims, which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.

In response to this rejection, Applicants assert that this rejection will be addressed with a terminal disclaimer, if appropriate, upon notification of patentable subject matter in the present application.

These arguments have been carefully considered, but are not found persuasive.

As stated above, although the conflicting claims are not identical, they are not patentably distinct from each other because the method claimed in the conflicting patent appears to fall within the same scope of the method claimed in the instant application.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

BF